Cognitive development in children with Prader–Willi syndrome

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INTRODUCTION

The disease was first described by the Swiss pediatricians A. Prader and H. Willi in 1956. At present, the estimated incidence of Prader–Willi syndrome (PWS) in Europe is 1:30 000 live births, in the general population - 1:50 000.[¹] The PWS has characteristic features that in the most patients can be detected during the first 6 months of life, which will allow timely correction of metabolic and hormonal disorders and to improve the quality of life. The damage to the same area of chromosome 15 is also observed in Angelman syndrome, the clinical picture of which is significantly different from PWS: The early (aged 6–12 months) retardation of psychomotor development, microcephaly, speech impairment (in 100% cases), ataxia, uncontrolled violent laughter, frequent epileptiform seizures, and specific facial expression. The development of these diseases is associated with new genetic phenomena (genomic imprinting and uniparental disomy).[²] To identify the syndrome, special cytogenetic and molecular genetic methods (prometaphase analysis, the use of DNA markers of the areas of chromosome 15) are used.

Despite the observations indicating that the loss of the paternal imprinted region of 15q11-q13 causes PWS and the identification of a variety of imprinted genes in this region, the exact cause of the disease is still not obvious, the specificity of the cognitive development in children with this syndrome is not described entirely, and the problem is actual at the moment.[³] There are a lot of researches connected with motor development in these children,[⁴,⁵] respiratory problems,[⁶] different ways of diagnostics[⁷] and hormone treatment are as follow: Growth hormone,[⁸,⁹] oxytocin,[¹⁰,¹¹] quality of life,[¹²] etc. The anthropometric and laboratory assessment of patients with PWS is actively carried out. There are some specific instruments for the assessment of children with PWS, such as PWS behavioral questionnaire[¹³] and hyperphagia questionnaire.[¹⁴]

ABSTRACT

Aim: The article is devoted to the specificity of cognitive development in three children with Prader–Willi syndrome (PWS) in the period up to 6-year-old. The PWS is a rare hereditary disease caused by the absence of the father’s copy of the 15q11-13 chromosome. Methods: Genomic imprinting is involved into the regulation of the genes in this area of chromosome 15. Diagnostic signs of this syndrome are muscular hypotension, hypogonadism, obesity, excessive adiposity, respiratory complications, mental retardation, small brushes and feet, dysplasia of the hip joints, and stigma of disembyrogenesis. Currently, specific ways of treating people with this syndrome have not been developed. It is considered that children with PWS suffer from the retardation of cognitive development; however, there is a lack of scientific information about it. The study of PWS requires an interdisciplinary approach and the detailed description of cognitive development. Results: The results showed that in the period up to 6 years in three children with this rare syndrome the most obvious decline is registered predominantly in the development of expressive speech, and other functions do not suffer significantly in spite of the presence of impairments in motor development. Conclusion: The research was conducted at A. Yu. Ratner Pediatric Clinical Hospital NO. 8 (Kazan, Russia) by the group of clinical linguists, neurologists, and speech therapists.

KEY WORDS: Assessment of cognitive functions, Clinical linguistics, Developmental disorders, Prader–Willi syndrome

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Within the framework of the project “clinical linguistics,” the children with PWS receive complex rehabilitation. Two boys (B-1 and B-2) and one girl (G-1) with PWS were diagnosed and treated in the period from two till 6-year-old. The group of clinical linguists, neurologists, and speech therapists assessed physical development and the development of cognitive functions in these children.

**MATERIALS AND METHODS**

The research was conducted at A. Yu. Ratner Pediatric Clinical Hospital No. 8 (Kazan, Russia), the data were processed in the laboratory “clinical linguistics” (Kazan Federal University).

Before the assessment of cognitive functions, two boys performed within the normal range on the Raven’s Progressive Matrices. The girl was too small for these matrices, and the level of her development was assessed with the help of Mac Arthur Communicative Development Inventories (MacArthur CDI – the Russian version). The development of cognitive functions was assessed with reliance on the principles of neuropsychological diagnosis worked out for children by T. V. Akhutina and with the help of subtests created in Kazan Federal University. We assessed functions of programming, regulation, and control; visual gnosis; visual-spatial gnosis; functions of the auditory analyzer; functions of the kinesthetic analyzer; impressive speech and expressive speech; general adaptive skills; development of hand motor skills; executive functions; emotion recognition; and the specificity of behavior.

Children were subjected to an electroencephalographic (EEG) study according to a standard procedure using the international electrode arrangement “10–20” in bipolar installation. The recording of the EEG was performed in wakefulness and daytime sleep on the 19-channel computer EEG-A-21/26 encephalan-131 M (research and production company Medicom-MTD, Taganrog).

**RESULTS**

The described three children are comparable by their age, neurological status, and the level of motor functions retardation. In all children video, EEG-sleep monitoring revealed no epileptic activity. All of them have diffuse muscular hypotension from the early neonatal period. In the process of motor development, all of them had problems: They did not roll over and crawl during the 1st year of their life, they became able to sit with severe retardation, and began to walk without help when they were in the period from 2 to 3-year-old. They are not able to run, to jump, they have problems with walking upstairs and downstairs and characterized by a significant motor awkwardness. B-1 walks with a broad base of support, G-1 has dysplasia of the hip joint, and congenital flexion contracture of 3-5 fingers on the right hand. B-1 and G-1 had the 2nd degree of cerebral ischaemia in their early neonatal periods. Only B-1 is observed by the endocrinologist because of exogenously-constitutional obesity (fat deposition is mainly observed on the torso and proximal parts of limbs), B-2 and G-1 do not have such a problem. In two boys, B-2 has bilateral cryptorchidism, B-1 has no problems of such kind. It is important to mention that B-2 demonstrates the greatest delay in the development of cognitive functions (especially speech) in these three children despite his motor development is better and despite he does not have cerebralischaemia of the 2nd degree in his anamnesis.

In general, the understanding of speech is present in B-1 and G-1 at all language levels. Passive vocabulary is characterized by the presence of not only the main parts of speech but also by the service parts. There is also an understanding of such complicated grammar categories as the verb tense and aspect in B-1. Compound syntactic structures are available for them. B-2 shows less understanding of speech, he has a high score mainly on subtests related to the performance of common tasks, has a mild semantic-phonological deficit. B-2 is characterized by the low degree of motivation to study, reduced attention, and a high degree of hyperactivity; however, in everyday exercises and in different games, he is successful.

The functions of programming, regulation, and control are developed in B-1 and G-1 within normal range and lacking in B-2 as he has a low level of motivation to habilitation. Hence, the executive functions in B-1 and G-1, including neatness skills, are developed better (within the normal range). Visual and visual-spatial gnosis is not problematic in three children. Subtests on the auditory and kinesthetic analyzer did not reveal any significant deficit; however, it is necessary to mention that subtests on visual memory demonstrated higher results than subtests on auditory memory. General adaptive skills are normal in B-1 and G-1, B-2 has a mild deficit in this sphere.

**DISCUSSION**

It is traditionally indicated that in children with PWS, behavioral disorders such as hysteria, stubbornness, obsessive-compulsive manifestations, and rigidity of thinking are common. However, the observed three children do not demonstrate these disorders. The behavior of G-1 corresponds to the typical behavior for this age. B-1 demonstrates the high level of desire to communicate - active in social life, playful, well-developed emotionally, able to understand jokes,
and responsive to praise. B-2 has specific features in behavior determined by attention deficit hyperactivity disorder which is his confirmed diagnosis.

CONCLUSIONS

The authors come to the conclusion that despite the presence of the retardation in motor development, the described children with PWS do not have a significant complex delay in their mental development at the period up to 6 years. The visual-spatial and visual gnosia in them is developed within the normal range. There is also no significant deficiency of the auditory analyzer. The auditory memory is sufficiently developed (but the level is lower than visual). The development of the functions of programming, regulation, and control varies depending on the child’s motivation to get the new information (high motivation in B-1 and G-1 and low in B-2). The expressive speech in children with this syndrome is close to the age norm or becomes close to it in the course of habilitation work. During the year of habilitation work, there is progress in understanding the speech of all three children. However, expressive speech develops with a significant delay and for a very long time is at the stage of onomatopoeic and poor verbal speech, despite complex habilitation measures. Defects of tooth enamel and caries early lead to loss of teeth, hypotension affects the muscles of the articulatory apparatus, and therefore, the distinctness of articulation is severely affected, which further worsens the expressive speech and retard the cognitive development. The authors also suppose that there is a need in the specific standardized instrument for quantitative and qualitative assessment of cognitive functions in children with PWS (such as PWS behavioral questionnaire and hyperphagia questionnaire).

The results of the study can be used in clinical practice (in diagnosis and treatment of diseases connected with speech and cognitive disorders in children).

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